Available online on 15.01.2020 at http://jddtonline.info

Journal of Drug Delivery and Therapeutics

Open Access to Pharmaceutical and Medical Research

Open Access Research Article

In-Vitro Comparative Dissolution Study of Commercially Available Paracetamol Tablet

Kar Ayan Kumar*[1,2], Kar Banhishikha[1]

[1] Department of Pharmaceutics, Calcutta Institute of Pharmaceutical Technology & AHS, Banitabla, Uluberia, Howrah-711316, West Bengal

[2] School of Pharmacy, Techno India University, Salt Lake, West Bengal

ABSTRACT

Quality is the most important issue in the pharmaceutical field due to the presence of a drug which is considered as safe and therapeutically active agent. In-vitro evaluation ensures their quality, bioavailability as well as optimum therapeutic activity. Paracetamol (acetaminophen) which are the active metabolites of phenacetin is commonly used for the relief of headaches and pains, and is a major ingredient in numerous cold and flu remedies. Paracetamols are available in different brands in Indian market. The main objective of the present study was to conduct the comparative in-vitro dissolution studies of various brands collected from the local market to determine whether all the formulations used were equivalent or significantly different. The calibration curve was constructed covering the concentration range of 1 to 10 mcg/ml at 268 nm by UV spectrophotometer (UV 2203 Double beam spectrophotometer, Shimadzu). Five different brands of Paracetamol of 500 mg conventional tablets from different manufacturers were selected in the study and dissolution testing in Phosphate buffer at pH 7.4 was conducted from each brands for 90 mins by using dissolution testing apparatus USP type-II. The dissolution rate was subjected to various mathematical models like zero order, first order, Higuchi and Hixson-Crowell equations to elucidate the kinetic behavior of drug release from the test samples. Different release kinetics model of all the selected brands was assuring the quality standard of manufacturing.

Keywords: Paracetamol, Marketed Tablet, In-Vitro dissolution study, Release profile.

Article Info: Received 18 Nov 2019; Review Completed 13 Dec 2019; Accepted 20 Dec 2019; Available online 15 Jan 2020

Cite this article as:

Kar AK, Kar B, *In-Vitro* Comparative Dissolution Study of Commercially Available Paracetamol Tablet, Journal of Drug Delivery and Therapeutics. 2020; 10(1):18-23 http://dx.doi.org/10.22270/jddt.v10i1.3817

***Address for Correspondence:**

Kar Ayan Kumar, Department of Pharmaceutics, Calcutta Institute of Pharmaceutical Technology & AHS, Banitabla, Uluberia, Howrah-711316, West Bengal

INTRODUCTION:

Oral dosage form like tablets, capsules, suspensions etc is one of the most common method used for the administration of drug.. Among all, tablets are more widely used being tempered free, cost effective, and stable. In formulation systems, manufacturing process and raw materials used affects the quality of finished product. It is very much essential to determine the parameters of tablets to ensure the quality of the product. Quality of the finished product depends upon the early developmental process. A tablet contains a drug molecule and excipients which are used mainly to maintain the physical parameters as well as to control the release of drug from its dosage from. For a single generic drug, various brands are available. Quality of all available brands needs to be assessed in order to provide an efficacious formulation, this responsibility increases in case of over the counter (OTC) medicines, quality of the product vary from manufacturer to manufacturer [1].

Paracetamol, a widely prescribed Non-steroidal anti-inflammatory drug (NSAID) is used for the relief of pains associated with many parts of the body. Chemically, it is 4-hydroxy acetanilide (acetaminophen) which belongs to the non-salicylate analgesic group. This drug which has well-established metabolic and pharmacokinetic (pK) profiles is a universally accepted analgesic and antipyretic drug. It is poorly aqueous soluble and its frequency of administration is high due to low bioavailability [2,3].

Paracetamol has analgesic properties comparable to those of aspirin, while its anti-inflammatory effects are weaker. It is better tolerated than aspirin in patients in whom excessive gastric acid secretion or prolongation of bleeding time may be a concern. Available without a prescription, it has in recent years increasingly become a common household drug.[4]

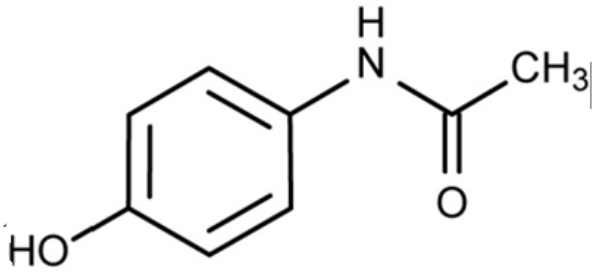

Fig. 1: Structure of Paracetamol [4]

Dissolution test, a qualitative and quantitative tool is one of the *in vitro* tests help to operate the quality of oral pharmaceutical solid dosage forms such as tablets and capsules. This test gives some important information about the biological availability of a drug and also batch to batch consistency of products [5].

The quality of marketed drugs determines the conditions of the patients treated. On the other hand, health condition of a consumer can be put at risk by the use of substandard drugs. So, continuous segregating process should be needed by the consumer organization for the awareness about the quality of drug available. Specially, some small and medium pharmaceutical industries do not analyse their drug or product properly before marketing due to the high expense for maintaining the quality control [6].

Therefore, it was decided to carry out the comparative evaluation of *in vitro* dissolution qualities of various commercially available paracetamol tablet samples. Paracetamol tablets of 500 mg were chosen for the study. Statistical assessment of various *in vitro* dissolution parameters was conducted to establish if there were any significant differences among them.

MATERIALS AND METHOD:

Materials:- Paracetamol tablets (500 mg) were collected from the local market in west Bengal from the different company which is given in Table 1. All other ingredients were taken as an analytical grade.

Table 1: List of collected marketed paracetamol tablet

Sl. No.	Brand Name	Company Name	Manufacturing date	Expiry date	Batch code
	Apex 500	Apex Lab. Pvt Ltd	24.01.2019	28.11.2021	F - A
	Crocin 500	Remidex Pharma Pvt Ltd	17.02.2019	21.12.2021	F - B
	Calpol 500	GlaxoSmithKline	10.08.2019	21.11.2021	F - C
	Pyrigesic 500	East India Pharma	18.08.2019	19.11.2021	F - D
	Arden 500	Adonis Lab. Pvt. Ltd.	14.05.2019	16.12.2021	F - E

Methodology:

Preparation of Phosphate buffer at pH 7.4 [7]:

Dissolve 27.218g of potassium di-hydrogen phosphate and 7.99g of sodium hydroxide in sufficient distilled water containing in the 1000ml volumetric flask and to make up to the volume 1000ml.

Place 50ml of 0.2 M Potassium di-hydrogen phosphate in a 200ml volumetric flask, add the specified volume of 0.2 M sodium hydroxide and then add distilled water to make up the volume 200ml.

Preparation of calibration curve of paracetamol [8]:

Stock solution of drug (1mg/ml) is prepared by dissolving 100 mg of drug in 100 ml solution of phosphate buffer pH 7.4 in 100 ml volumetric flask (to get 1000 µg/ml drug solutions) with vigorous shaking. A aliquot sample (10 ml) from previous stock is diluted to 100 ml with phosphate buffer pH 7.4 to get a stock solution to get a concentration of 100 µg/ml of drug. The stock solution was filtered through Whatmann filter paper No.41. The respective samples at the range of .1 ml to 1ml was taken in each test tube separately and diluted with phosphate buffer pH 7.4 to make the total volume upto 10 ml to make a concentration range 1 to 10 mcg/ml. The standard solutions for the drug having concentration 1, 2, 3, 4, 5, 6, 7, 8, 9 and 10 µg/ml was prepared with phosphate buffer pH 7.4 from the stock solution. A calibration curve was plotted between absorbance v/s concentration to get the linearity and regression equation.

In vitro dissolution study [8]:

Dissolution rate studies were performed in 900 ml of phosphate buffer at ph 7.4 at 37 ± 0.5 ^{0}C, using 6-station USP type-II (paddle) apparatus with paddle rotating at 50 rpm. Different marketed 500 mg of Paracetamol tablet was placed in dissolution basket. At fixed time intervals, samples withdrawn were filtered and spectrophotometrically analysed for the drug content at 268 nm. The rate of drug release at different time interval was calculated and the kinetics of drug release was analysed according the different kinetics models like zero order, first order, higuchi model etc.

RESULT AND DISCUSSION:

A UV absorption maximum was determined by scanning 10µg/ml solution of paracetamol in phosphate buffer 7.4, in between 200-400 nm by using UV-visible spectrophotometer. Further a representative spectrum was drawn of paracetamol in phosphate buffer pH 7.4. The absorbance of solutions of pure paracetamol drug were measured at 268 λ max shown in table 2 and a calibration curve was plotted with the regression value 0.999 shown in Fig. 2. The obtained regression value was indicating about the linearity between the concentration (Conc.) and absorbance (Abs.)

Table 2: Absorption profile of paracetamol

Conc. (mcg/ml)	Abs.
1	0.06
2	0.108
3	0.164
4	0.219
5	0.285
6	0.33
7	0.39
8	0.455
9	0.510
10	0.555

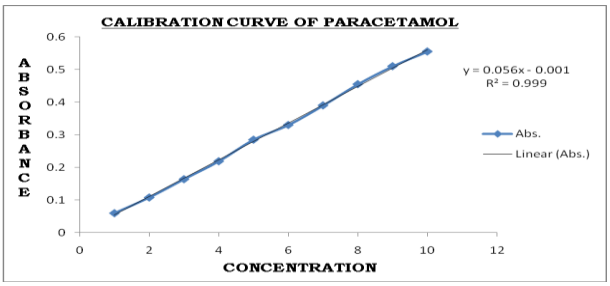

Fig. 2 : Calibration curve of paracetamol using phosphate buffer at 7.4

In-Vitro release study:

The *in vitro* dissolution studies of the marketed paracetamol tablets was carried out using USP type II apparatus (Electrolab, Mumbai, India) at 50rpm. The dissolution medium consisted of 900 ml of distilled water maintained at 37 ± 0.5°C. The drug release at different time intervals was measured using an UV visible spectrophotometer.

The dissolution rate was subjected to various mathematical models like zero order given in Table 3, first order given in Table 4, Higuchi model given in Table 5 and Krosmeyer Peppas model given in Table 6 and to elucidate the kinetics behaviour and mechanism of drug release from the different marketed tablets, data obtained from the release studies were fitted to various models shown in Fig. 3 to Fig. 6. The comparative evaluation of *in vitro* dissolution qualities of various paracetamol tablets was done by contrasting the values of regression coefficient given in table 7. After evaluating all of the data, it has been concluded that among all of the formulation, apart from F – A and F – E batch, all other batches was showing better regression coefficient. It was observed from the regression coefficient values that the release kinetics of' paracetamol from all the tablets appears to be almost uniform.

Table 3: Drug release data fitted to Zero order model

	Cumulative % drug release				
Time (min)	F - A	F – B	F – C	F – D	F - E
5	41.98	16.51	9.9	37.32	39.63
10	42.644	25.451	29.391	41.944	40.624
20	46.615	28.072	34.353	44.594	41.944
30	49.584	32.033	36.003	49.214	46.574
45	54.544	32.033	36.334	53.175	48.554
60	61.815	43.603	37.984	58.135	50.865
75	65.126	43.934	39.964	61.206	55.165
90	69.096	47.864	40.154	63.746	58.796

Fig. 3: Comparative zero order kinetics of different marketed paracetamol tablet

Table 4: Drug release data fitted to First order model

	Log cumulative % of drug retained				
Time (min)	**F - A**	**F – B**	**F – C**	**F – D**	**F - E**
5	1.763	1.921	1.958	1.797	1.78
10	1.758	1.872	1.848	1.763	1.773
20	1.727	1.856	1.817	1.743	1.763
30	1.702	1.832	1.806	1.705	1.727
45	1.657	1.832	1.803	1.67	1.711
60	1.581	1.751	1.792	1.621	1.691
75	1.542	1.748	1.778	1.588	1.651
90	1.49	1.717	1.777	1.559	1.614

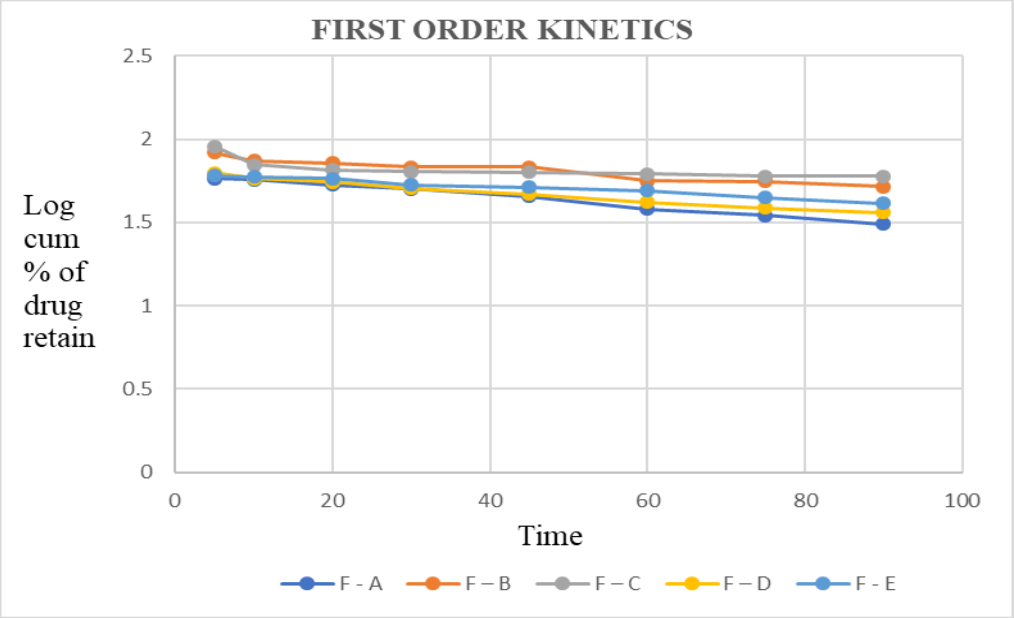

Fig. 4: Comparative First order kinetics of different marketed paracetamol tablet

Table 5: Drug release data fitted to Higuchi model

	Cumulative % of drug release				
Square root of time	**F - A**	**F – B**	**F – C**	**F – D**	**F - E**
2.236	41.98	16.51	9.9	37.32	39.63
3.162	42.644	25.451	29.391	41.944	40.624
4.472	46.615	28.072	34.353	44.594	41.944
5.477	49.584	32.033	36.003	49.214	46.574
6.708	54.544	32.033	36.334	53.175	48.554
7.745	61.815	43.603	37.984	58.135	50.865
8.66	65.126	43.934	39.964	61.206	55.165
9.486	69.096	47.864	40.154	63.746	58.796

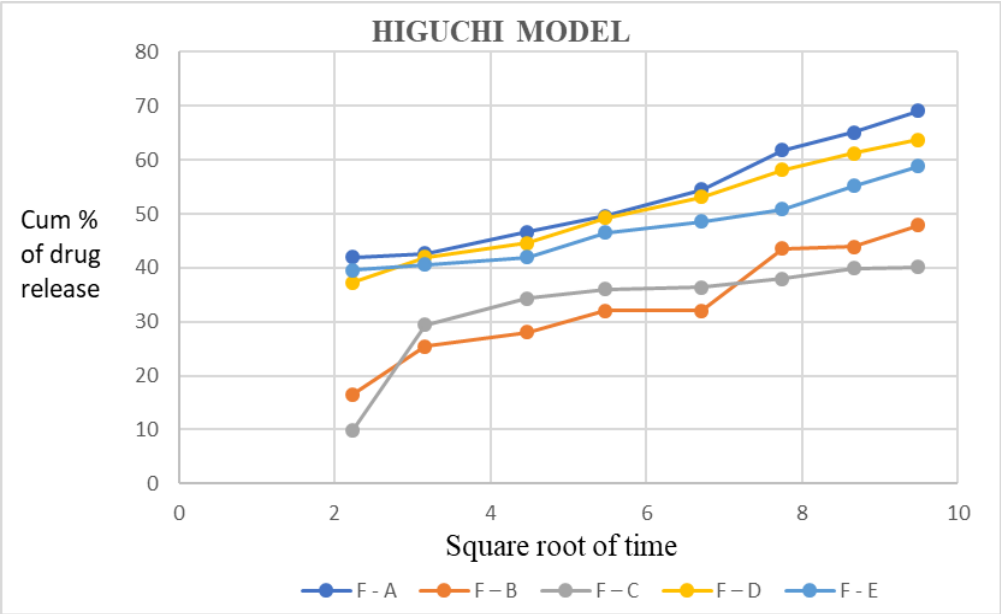

Fig. 5: Comparative Higuchi kinetics of different marketed paracetamol tablet

Table 6: Drug release data fitted to Krosmeyer peppas model

	Log cumulative % of drug release				
Log time (min)	**F - A**	**F – B**	**F – C**	**F – D**	**F - E**
0.698	1.623	1.217	0.99	1.571	1.598
1	1.629	1.405	1.468	1.622	1.608
1.301	1.668	1.448	1.535	1.649	1.622
1.477	1.695	1.505	1.556	1.692	1.668
1.653	1.736	1.505	1.56	1.725	1.686
1.778	1.791	1.639	1.579	1.764	1.706
1.875	1.813	1.642	1.601	1.786	1.741
1.954	1.839	1.68	1.603	1.804	1.769

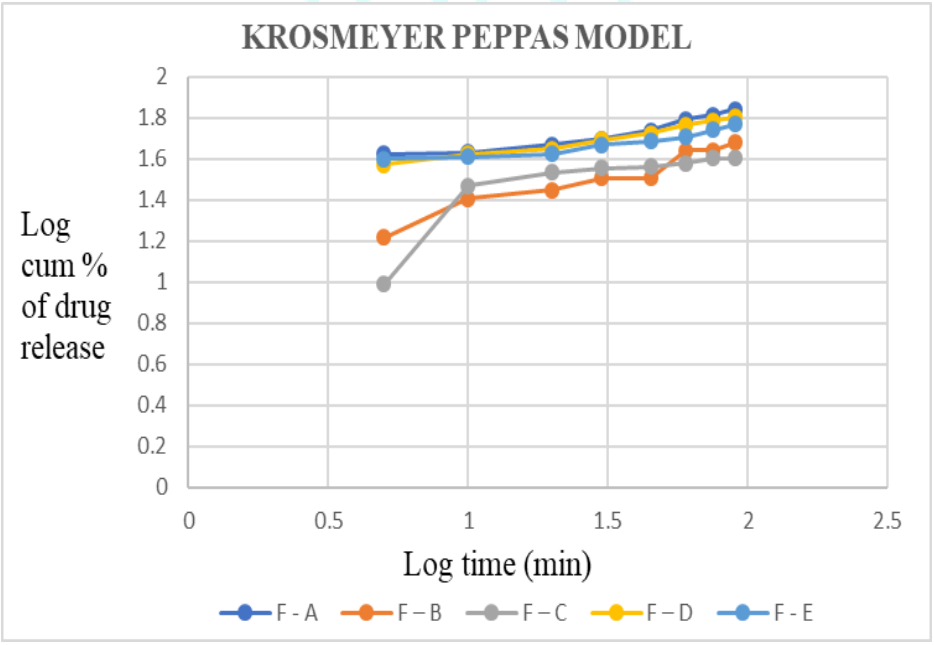

Fig. 6: Comparative Krosmeyer peppas kinetics of different marketed paracetamol tablet

Table 7: Comparison of regression coefficient of different kinetics model

Batch Code	Zero order	First order	Higuchi model	Krosmeyer peppas model
F - A	0.972	0..573	0.969	0.903
F – B	0.993	0.938	0.995	0.975
F – C	0.988	0.994	0.960	0.892
F – D	0.920	0.989	0.945	0.994
F - E	0.532	0.991	0.664	0.692

CONCLUSION:

Bioavailability and absorption of drug is dependent on dissolution profile. A dissolution study gives an idea about the amount of drug available for absorption after oral administration. In the present study, the release of paracetamol from all tablets, specially F – C batch (Crocin 500) was followed sustained release; though the drug release in 60 mints were almost about 60% which meets BP Specifications.

REFERENCES:

1. Qureshi M S, Rukh G, Kirplani P D, Farheen A, Hamid M. A comparative study of quality on conventional paracetamol tablets available in Pakistan. Research in Pharmacy and Health Sciences, 2016; 2(3): 205 – 210.
2. Sowjanya S P, Madhavi C H, Sowjanya D, Girisha D, Deeraj D, Vidya D S. Formulation and enhancement of dissolution rate of paracetamol tablets employing selected binders and disintegrants as per 22 factorial design. Indian Journal of Pharmaceutical Science & Research, 2016; 6(2): 73 -77.
3. Sultana R, Sarker K and Sultana S. Preparation and evaluation of paracetamol effervescent tablets under normal and exaggerated storage conditions. Bangladesh Pharmaceutical Journal, 2014; 17(1): 75 – 78.
4. Aulton M E. Aulton's Pharmaceutics : The Design and manufacture of Medicines, 2nd edition, Churchill livingstone, 1987.
5. Ghayas S, Sheraz M A, Anjum F, Baig M T. Factors influencing the dissolution testing of drugs. Pakistan Journal of Health Research, 2013; 1(1): 1 – 11.
6. The Indian Pharmacopoeia, Government of India, Ministry of health and family welfare, Controller of publication, New delhi, vol. II, 1996, A80 – A84.
7. Ahmida N H S, Abu – Naja M S, Doghman Y S A. Determination of paracetamol in tablet by Different Spectrophotometric Method. Asian Journal of Chemistry, 2009; 21(3): 2233 – 2240.
8. Kumar C S P, Ratna J V, Aditya P, Raakhiya SK, Sunitha S V, Revathi S. Formulation and evaluation of fast dissolving tablets of paracetamol using oats powder. International Journal of Pharmaceutical Science Invention, 2016; 5(3):7 – 12.